Infection by H1N1 flu virus revealing T-cell acute lymphoid leukaemia: about two cases

Guillaume Lefevre • Jean-Christophe Ianotto •
Adrian Tempescul • Philippe Lemoine •
Gaelle Guillerm • Christian Berthou

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Dear Editor,

We present here two exceptional cases of young patients who developed pulmonary infections due to the H1N1 flu, which revealed the presence of T-cell acute lymphoid leukaemia. In late 2009, a 16-year-old woman, and 2 weeks later, a 12-year-old boy were admitted to our hospital for pulmonary syndrome associated with high fever. The clinical presentation was similar for both patients: asthenia, high fever, cough, rhinorrhea and dyspnoea, but no thoracic pain. The two patients needed oxygen therapy. Chest X-rays of both patients showed bilateral interstitial syndrome and right basal condensation. Computed tomography (CT) scans confirmed the bilateral alveolar condensation syndrome with an air bronchogram, ground glass opacities and numerous fuzzy nodules (Fig. 1). The two CT scans revealed multiple mediastinal adenopathies and a large thymus. The H1N1 flu virus was suspected because of the epidemic in the winter of 2009. The diagnosis was confirmed by real-time PCR using the H1SWL test (M-CNR Pasteur gene) with the LightCycler 2.0 (Roche) and bronchoalveolar lavage fluid from the girl and nasal liquid from the boy. Due to the high fever and neutropaenia, the

patients were immediately treated with antibiotics and cefotaxime (ciprofloxacin and cefotaxime for the girl; cefotaxime, josamycin and amikacin for the boy), but with little success. After the diagnosis of H1N1 flu infection, we used oseltamivir at the recommended dose of 75 mg per day (from day 3 for the first patient and day 1 for the boy). The symptoms disappeared a few days after beginning the oral treatment, and oxygen was no longer needed. Oseltamivir treatment was stopped after 5 days.

During this time, we observed cytopaenias in the haemograms of both patients. For the girl and boy, the haemoglobin levels were 77 and 44 g/L, platelets were 224 and $61 \times 10^9/L$, white blood cells were 17.1 and $1.9 \times 10^9/L$, and polymorphonuclear neutrophils were 0.34 and $0.42 \times 10^9/L$, respectively. Blood exams showed the presence of medium-size blasts quantified at 14.5 and $0.8 \times 10^9/L$ for the girl and boy, respectively. We observed 3% of circulating CD4+ T-cell lymphocytes for the girl and none for the boy. The LDH levels were 585 and 728 UI/L, respectively. C-reactive protein was 34 and 202 mg/L. The diagnosis of T-ALL was made based on examination of the bone marrow: the infiltration of blasts was higher than 90%, with sizes ranging from medium to large; the nucleo-cytoplasmic ratio was elevated; the cytoplasm was hyperbasophilic with no granulations. Examination of the blasts, using flow cytometry, confirmed that they were of T-cell origin. The karyotypes were normal. The final diagnosis of type II T-ALL was made for both patients. When the pulmonary symptoms disappeared, we introduced chemotherapy using the same induction therapy for both patients: corticosteroids alone for the first week, and thereafter, corticosteroids together with vincristine, daunorubicin, cyclophosphamide and asparaginase. Intrathecal injections of chemotherapy were given three times during induction, and no meningeal localisation of virus was observed. The presence of the H1N1 influenza virus did not influence the progress of the

Guillaume Lefevre and Jean-Christophe Ianotto have contributed equally to this work.

G. Lefevre • J.-C. Ianotto (✉) • A. Tempescul • G. Guillerm •
C. Berthou
Département d'Hématologie, Institut de Cancéro-hématologie,
Hôpital Morvan,
Avenue Foch,
CHRU Brest, France
e-mail: jcianotto@hotmail.com

P. Lemoine
Département de Pédiatrie, Hôpital Morvan,
Avenue Foch,
CHRU Brest, France

Fig. 1 CT scan confirmed the bilateral alveolar condensation syndrome with an air bronchogram, ground glass opacities and numerous fuzzy nodules

chemotherapy protocol. The girl was resistant to corticosteroids at day 8 and to chemotherapy at day 15. The boy was sensitive to both corticosteroids and chemotherapy. The two patients were in complete haematological remission at the end of the induction phase. They followed their therapy, and no additional lung infections occurred. They are still in complete remission and in treatment today.

The cases described here are exceptional, because in all previously reported cases of H1N1 influenza in leukemic patients, the virus infection appeared during the aplastic phase secondary to chemotherapy. There is only one reported case of the H1N1 flu in a patient with hemopathy: a 67-year-old man who developed an H1N1 infection during a chemotherapy (cyclophosphamide, vincristine and prednisolone) treatment for chronic lymphocytic leukaemia and died after 4 weeks [1].

In the cases reported here, the two patients had deep lymphopaenia at the time of diagnosis, which was probably present for many weeks. The first sign of T-ALL was the

presence of an H1N1 flu virus pulmonary infection, which was observed during the winter, pandemic of this virus. The association between lymphopaenia and the H1N1 flu virus has been previously shown, with a higher mortality in the patients with low count. No secondary infections were observed, and neither patient experienced acute respiratory distress syndrome (ARDS), perhaps due to the neutropenia, despite the fact that previously reported deaths were mostly due to ARDS [2, 3]. The only recommended treatment for the H1N1 virus is oseltamivir, and this treatment is highly effective [4–7]. We confirmed the efficacy in immunocompromised patients. In these two cases, the occurrence of the H1N1 flu virus did not result in modification of the treatment, nor the results of the chemotherapy as the two patients were alive 7 months after the diagnosis and in complete haematological remission. These cases suggest that H1N1 virus infections could be masking other conditions in immunocompromised patients, and they confirm that oseltamivir is effective in these patients.

Conflict of interest None.

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